Stereochemistry of the Tetrahydroisopimaric Acids: *X*-Ray Structure of Methyl 8α-Isopimaran-18-oate

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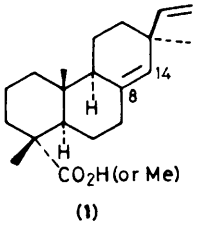
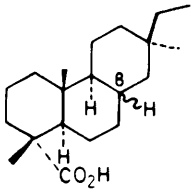
A second, previously unreported tetrahydro derivative has been isolated from the high pressure hydrogenation product of methyl isopimarate. Its structure is established as methyl 8α-isopimaran-18-oate by *X*-ray crystallography and ^{1}H n.m.r. spectroscopy.

Diterpene resin acids of the abietane, pimarane, and isopimarane type are the primary components of commercial rosins. In the course of isolating and purifying these acids and their hydrogenated derivatives to obtain standard spectra,[1] we discovered a second tetrahydroisopimaric acid hitherto unreported. Here we report the isolation and identification of this tetrahydroisopimaric acid, and compare it with the previously reported compound.

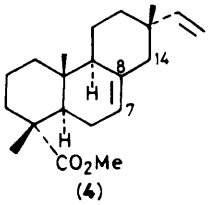
The hydrogenation of dihydropimaric acid with a platinum catalyst gives two different tetrahydro acids depending on the conditions used.[2] At ambient conditions, the *trans-anti-trans* (*t-a-t*) material, pimaran-18-oic acid (**2**), is the predominant component (65—70%) when pimaric acid (**1**), dihydropimaric acid, or the corresponding 8-ene acids are hydrognated. At high pressure and elevated temperature, the *trans-anti-cis* (*t-a-c*) material, 8α-pimaran-18-oic acid (**3**), predominates (we observed 60—70%). The stereochemistry of the *t-a-t* acid was determined[3,4] by synthetic sequences that did not affect the stereochemistry at C(8).



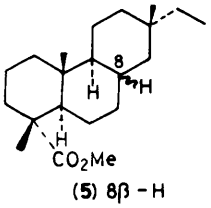
(1)



(2) 8β-H
(3) 8α-H



(4)



(5) 8β-H
(6) 8α-H

In an analogous fashion, two tetrahydroisopimaric acid products can be prepared by hydrogenation. One of them, assigned the *t-a-t* stereochemistry, was reported by Edwards and Howe[5] from hydrogenation of dihydroisopimaric acid at ambient conditions. We have observed that hydrogenation of methyl isopimarate (**4**), methyl 8,15-isopimaradien-18-oate, and sandaracopimarate [the endocyclic double bond in the 7, 8, and 8(14) position, respectively] gives 80—85% of the *t-a-t* ester, methyl 8β-isopimaran-18-oate (**5**). At high pressure and elevated temperature, however, the *t-a-t* and a second tetrahydroisopimarate, methyl 8α-isopimaran-18-oate (**6**), were produced in nearly equal amounts on hydrogenation of methyl isopimarate. The *t-a-c* configuration for this second tetrahydroisopimarate is indicated by the significant downfield shift of the C(20) (methyl) proton resonance, analogous to the shift differences between the *t-a-c* and *t-a-t* derivatives of the pimaranoates and abietanoates (Table 1). However, two other structural possibilities (based on the A–C *syn* configuration resulting from a 9α-H), although unlikely, are not rigorously excluded.

Table 1. Comparative ^{1}H n.m.r. data[a] for isopimaranoates, pimaranoates, and abietanoates ($CDCl_3$; δ values in p.p.m. from Me_4Si)

Compound (Me ester)	CO_2Me	19-Me	20-Me	17-Me	16-Me
			trans-anti-trans		
Pimaran-18-oate (**2**)	3.64	1.17	0.76	0.86	0.75,*d*
Isopimaran-18-oate (**5**)	3.64	1.18	0.80	0.88	0.79,*d*
Abietan-18-oate[b]	3.62	1.17	0.84	0.83,*d*	
13β-Abietan-18-oate[b]	3.63	1.16	0.84	0.85,*d*	
			trans-anti-cis		
8α-Pimaran-18-oate (**3**)	3.65	1.19	1.07	0.87	0.81,*d*
8α-Isopimaran-18-oate (**6**)	3.65	1.18	1.09	0.79	0.74,*d*
8α,13β-Abietan-18-oate[b]	3.62	1.18	1.06	0.84,*d*	
			trans-syn-cis		
9β,13β-Abietan-18-oate[b]	3.63	1.14	1.05	0.82,*d*	

[a] Obtained with Bruker spectrometer operated at 250 MHz. [b] From Zinkel *et al.*[1] (100 MHz).

The *X*-ray results show the molecular dimensions and geometry to be typical of saturated, fused cyclohexane ring systems (Figures **1a**—**c**). Rings B and C are fused *cis* in contrast to rings A and B which are fused *trans*; the A/C ring junction *via* the C(9)–C(10) bond is *trans*. The three rings have the preferred chair conformation but are distorted from ideal cyclohexane geometry because of ring fusion and the steric interaction of the substituents, especially the two axial methyl groups, C(19) and C(20). The C(19)–C(20) intramolecular contact is 3.292 Å. The interaction of the C(20) methyl group with atoms of ring C

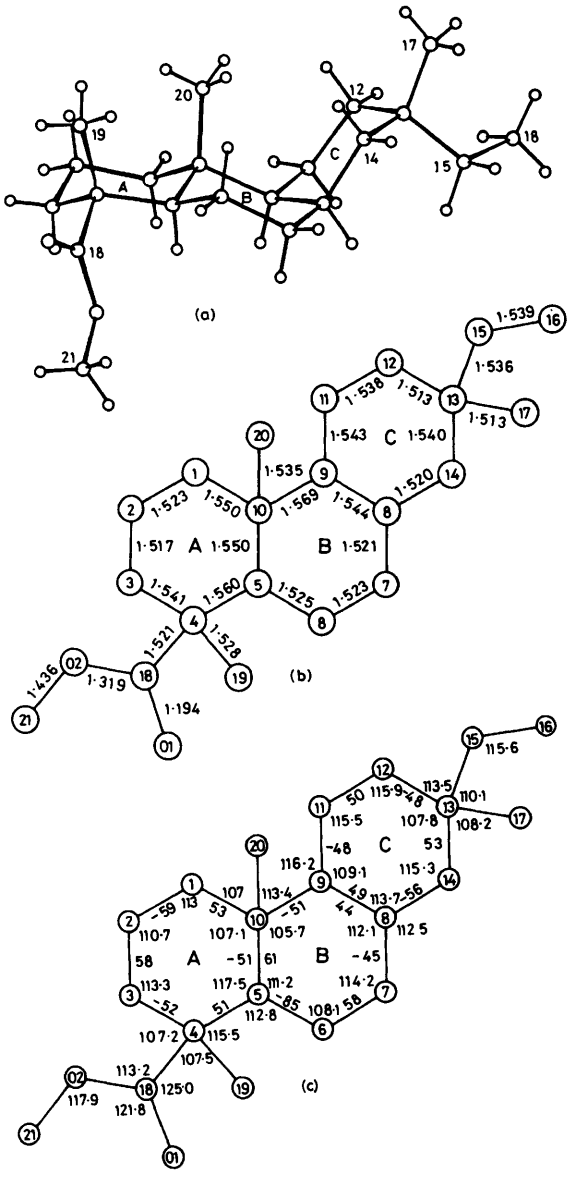


Figure. Methyl 8α-isopimaran-18-oate (**6**). (a) Perspective view of the molecular structure, (b) bond distances, and (c) bond angles and ring torsion angles. The mean e.s.d.s are 0.005 Å, 0.3° and 0.4° for these molecular parameters, respectively. Angles: C(1),C(10),C(9) = 108.6°; C(3),C(4),C(19) = 111.0°; C(5),C(4),C(18) = 107.0°; C(5),C(10),C(20) = 114.2°; C(12),C(13),C(17) = 107.9°; C(14),C(13),C(15) = 109.1°

causes additional strain. The C(20)–C(12) and C(20)–C(14) contacts are 3.334 and 3.443 Å, respectively. As a result, the central B ring is distorted from ideal geometry. The distortion can be accurately determined by calculating the Cremer-Pople[6] ring puckering parameters, Q and θ, where Q is the total amplitude of ring puckering and θ is the degree of chair (θ = 0° or 180°) versus boat (θ = 90°) character; a third parameter, φ, which is a measure of boat and twist-boat configuration is of less significance here. The respective values of Q, θ, and φ for each ring are: ring A, 0.554 Å, 4°, 46°; ring B, 0.569 Å, 15°, 5°; ring C, 0.511 Å, 175°, 123°. A perspective view of the molecule [Figure (a)] clearly shows the *cis* B/C ring junction. The C–C bond lengths are in the range 1.513—1.569 Å [Figure (b)], the longest bonds occurring between tertiary and quaternary carbon atoms. The bond angles range from 105.7° at C(10) to 125.0° at C(18) [Figure (c)]. The ring torsion angle magnitudes range from 44 to 65° [Figure (c)] with most of the values less than 60°, the value for an ideal chair. Thus all the rings are somewhat flattened. The only intermolecular contact less than 3.6 Å is between O(1) and C(21) of a screw-related molecule with a distance of 3.098 Å.

Table 2. Fraction co-ordinates (× 10^4) for the carbon and oxygen atoms of methyl 8α-isopimaran-18-oate (**6**)

Atom	*x/a*	*y/b*	*z/c*
C(1)	7 011(3)	5 526(6)	718(2)
C(2)	5 930(3)	6 850(7)	478(2)
C(3)	5 521(3)	6 828(7)	1 446(3)
C(4)	6 432(2)	7 619(5)	2 516(2)
C(5)	7 565(2)	6 372(5)	2 704(2)
C(6)	8 518(2)	6 967(6)	3 770(2)
C(7)	9 414(3)	5 225(7)	4 086(2)
C(8)	9 909(2)	4 689(5)	3 204(2)
C(9)	8 968(2)	4 514(5)	2 059(2)
C(10)	8 021(2)	6 266(5)	1 740(2)
C(11)	9 538(3)	4 044(6)	1 206(2)
C(12)	10 587(3)	5 408(7)	1 292(3)
C(13)	11 499(2)	5 567(6)	2 420(3)
C(14)	10 898(3)	6 123(6)	3 236(3)
C(15)	12 192(3)	3 535(7)	2 796(3)
C(16)	12 945(3)	2 883(9)	2 131(4)
C(17)	12 292(3)	7 360(8)	2 405(4)
C(18)	6 016(2)	7 043(6)	3 447(2)
C(19)	6 541(3)	10 010(6)	2 508(3)
C(20)	8 445(2)	8 377(6)	1 457(2)
O(1)	5 711(2)	8 272(5)	3 981(2)
O(2)	6 005(2)	5 000(0)	3 613(2)
C(21)	5 639(3)	4 280(8)	4 482(3)

The *X*-ray crystallographic results provide unambiguous evidence for a *t-a-c* backbone configuration, confirming the assignments based on ^{1}H n.m.r. data. The absolute configuration of (**6**) is based on the known stereochemistry of the related sandaracopimaric acid.[7]

Experimental

Isolation of Tetrahydroisopimarates.—Methyl isopimarate (130 mg) in acetic acid was hydrogenated with PtO_2 catalyst for 24 h at 60 °C and a pressure of 700 KPa to give a product composed of a mixture (*ca.* 1:1) of two tetrahydroisopimarates. Preparative g.l.c. using a 26 ft × ¼ in column containing 3% SE-30 on Anakrom ABS packing provided methyl isopimaran-18-oate (**5**) and methyl 8α-isopimaran-18-oate (**6**), both with a purity of 99%. Methyl isopimaran-18-oate was recrystallized from methanol, m.p. 69.5—70 °C (evac. cap., corr.; lit.,[5] 68—69 °C); $[\alpha]_D^{25}$ 11° (*c* 0.4, $CHCl_3$; lit.,[5] $[\alpha]_D$ 18°). Methyl 8α-isopimaran-18-oate was also crystallized from methanol, m.p. 67—68 °C (evac. cap., corr.); $[\alpha]_D^{25}$ 17° (*c* 0.4, $CHCl_3$). I.r., m.s., n.m.r., and g.l.c. retention (packed column) data are recorded.[1] Capillary g.l.c. data have been published,[8] but the data for the two tetrahydroisopimarates for SE-30 are reversed, both at 170 and 190 °C.

Crystal Data.—Compound (**6**), $C_{21}H_{36}O_2$, M = 320.49 crystallizes in the monoclinic system with unit cell constants a = 12.435(3), b = 6.366(1), c = 13.032(2) Å, and β = 110.51(3)°, and V = 996.24 Å^3. Unit cell parameters were refined by a least-squares algorithm using 25 automatically centred reflections. *X*-Ray intensity data were collected on an Enraf-Nonius CAD-4 diffractometer using Ni-filtered Cu-K_α radiation (λ = 1.5418 Å). The space group is $P2_1$ with Z = 2 and D_x = 1.10 g cm^{-3}.

The crystals were colourless needles. The crystal used for data collection had dimensions of 0.5 × 0.1 × 0.05 mm. The linear absorption coefficient, $\mu(\text{Cu-}K_\alpha) = 5.30\ \text{cm}^{-1}$.

A total of 2 004 unique reflections were measured up to a 2θ limit of 150°, of which 1 604 were classed as observed [significantly above background, or $>2\sigma(I)$]. Only the observed reflections were used for the structure analysis. The data were corrected for crystal decay, *X*-ray absorption (using an empirical absorption correction based on variation both in 2θ and φ), as well as for Lorentz and polarization effects.

Initial attempts to solve the structure using MULTAN[9] were unsuccessful. A Patterson map revealed the ring C–C vectors for the fused A and B rings which were subsequently used to define the orientation of the structure. When this correctly orientated structure was used as input to MULTAN, sufficiently correct phases were obtained to allow the determination of the structure. The atomic co-ordinates were refined by the full-matrix least-squares method to a final *R*-index of 0.049 with non-hydrogen atoms refined with anisotropic temperature factors and hydrogen atoms refined with a fixed isotropic temperature factor of 4.0 Å^2. Scattering factors for carbon and oxygen are from Cromer and Waber,[10] and those for hydrogen are from Stewart *et al.*[11] Final non-hydrogen atom co-ordinates are listed in Table 2. Computer programs except for MULTAN were generated locally. Anisotropic temperature factors for non-hydrogen atoms, and the refined hydrogen atom co-ordinates are available on request from the Cambridge Crystallographic Data Centre.*

* See Instructions for Authors (1987), *J. Chem. Soc., Perkin Trans. 1*, 1987, Issue 1.

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